

METHOD FOR ALTERING UNDESIRABLE IMMUNE RESPONSES TO POLYPEPTIDES

ABSTRACT OF THE DISCLOSURE

Disclosed is a method for altering undesirable immune responses by identifying mutant polypeptides that exhibit less of an undesirable immune response while retaining one or more desired characteristics. Such polypeptides are safer and can be more efficacious when introduced into a human, other mammal, or other animal. Either the altered immune response or a surrogate for the immune response, referred to as a measurable immune characteristic, can be assessed in the method. Generally, the measurable immune characteristic can itself be an undesirable immune response, the measurable immune characteristic can be involved in an undesirable immune response, and/or an undesirable immune response can be mediated by the measurable immune characteristic. The disclosed method involves providing a collection of mutant polypeptides where the amino acid sequence of each mutant polypeptide differs in at least one position from a polypeptide of interest, identifying mutant polypeptides that exhibit less of the immune response than the polypeptide of interest, and identifying mutant polypeptides with less potential for eliciting an undesirable immune response that still retain the desired characteristic(s). The collection of mutant polypeptides can be provided by mutagenizing nucleic acid encoding a polypeptide of interest and expressing the mutagenized nucleic acid to produce mutant polypeptides. The method is especially useful for reducing immune responses involving both linear and/or conformational epitopes on a polypeptide of interest. This is possible because the recombinant polypeptides used as substrates for mutagenesis in the method are essentially full length, remaining structurally similar to the polypeptide of interest and displaying essentially the same conformational epitopes.

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